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REstart or STop Antithrombotics Randomised Trial

Submission date 24/04/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 25/04/2013	**Overall study status** Completed	
Last Edited 19/11/2024	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
More than one third of the adults with a stroke due to bleeding into the brain - known as brain haemorrhage - are taking drugs to prevent clotting when they have a brain haemorrhage. These patients had previously suffered illnesses like angina, heart attack, or stroke due to blood vessel blockage, which is why they are treated with drugs to prevent further clots occurring. These drugs are usually stopped when the brain haemorrhage occurs. But when patients recover from brain haemorrhage, they and their doctors are often uncertain about whether to restart these drugs to prevent further clots occurring, or whether to avoid them in case they increase the risk of brain haemorrhage happening again. We will study the potentially beneficial effects of three antiplatelet drugs (aspirin, clopidogrel, or dipyridamole) on the risks of heart attack, stroke and other clotting problems as well as their effect on the risk of a brain haemorrhage happening again. This information will help us to decide whether antiplatelet drugs are a promising treatment. If they are, we will recruit a much larger number of patients so that we can determine really reliably whether the beneficial effects of antiplatelet drugs on the risk of clotting outweigh any risks of a repeat brain haemorrhage for such people.

Who can participate?
We aim to recruit 720 men and women in the UK aged 18 years or more who survive a brain haemorrhage. If participants are unable to provide fully informed consent a relative or other legal representative may be approached for their consent.

What does the study involve?
Research staff will collect baseline information about each participant. Some participants may also have an additional MRI scan. Participants will be randomly allocated to either start or avoid antiplatelet medication. Over a period of at least two years we will collect information about participants progress, any medical problems and their adherence to the randomised treatment allocation (start or avoid antiplatelet medication). This follow up information will be obtained from participants, relatives and General Practitioners.

What are the possible benefits and risks of participating?
We do not know whether taking or avoiding antiplatelet medication is best, but participants have a chance to be exposed to the benefit of one or other strategy by participating. Some

people find it beneficial to be part of a research study and to be under regular follow-up. The results of this study will help us to treat patients better in future. Participants may find the time spent completing one questionnaire each year inconvenient. Participants, who have agreed to have an MRI scan, may become claustrophobic in the MRI scanner - if this happens the scan would be stopped. Because MRI scans are so detailed, there is also a 1 in 37 chance of finding an abnormality on your MRI scan that is completely incidental to your brain haemorrhage.

Where is the study run from and how long will it last?
RESTART is run by a team at the Division of Clinical Neurosciences at the University of Edinburgh, UK and it will last for at least five years.

When is the study starting and how long is it expected to run for?
Recruitment started on the 2nd May 2013 and will continue until 31st May 2018. Follow-up of these participants will be at least 6 months.

Who is funding the study?
RESTART is funded by the British Heart Foundation

Who is the main contact?
The UK Chief Investigator is Rustam Al-Shahi Salman and the Trial Manager is Karen Innes, and they can be contacted via RESTART.trial@ed.ac.uk.

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2012-003190-26

Protocol serial number
14297

Study information

Scientific Title
REstart or STop Antithrombotics Randomised Trial

Acronym
RESTART

Study objectives
For adults surviving spontaneous (non-traumatic) intracerebral haemorrhage (ICH) who had taken an antithrombotic (i.e. anticoagulant or antiplatelet) drug for the prevention of vaso-occlusive disease before the ICH, does a policy of starting antiplatelet drugs result in a beneficial net reduction of all serious vascular events over at least two years compared with a policy of avoiding antiplatelet drugs?

More details can be found at: www.restarttrial.org

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland A Research Ethics Committee, 02/11/2012, ref: 12/SS/0138

Study design
Interventional multicentre parallel group prospective randomised open blinded end-point (PROBE) clinical trial, Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Intracerebral haemorrhage

Interventions
1. Patients will be randomised to either 'start antiplatelet medication' (restricted to the use of one or more of aspirin, dipyridamole or clopidogrel at the investigator's discretion) or 'avoid antiplatelet medication'.
2. Additional pre-randomisation brain MRI (for patients participating in the MRI sub-study)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Aspirin, dipyridamole, clopidogrel

Primary outcome(s)

Current primary outcome measures as of 26/06/2017:
1. Recurrent symptomatic ICH
2. Fatal or non-fatal radiographically- or pathologically-proven recurrent symptomatic

Measured at least 6 months after baseline, detected using annual general practitioner and participant follow-up, with independent, blinded adjudication of the clinical information and investigations relating to every reported outcome

Previous primary outcome measures:
1. Recurrent symptomatic ICH
2. Fatal or non-fatal radiographically- or pathologically-proven recurrent symptomatic

Measured over 2 years after baseline, detected using annual general practitioner and participant follow-up, with independent, blinded adjudication of the clinical information and investigations relating to every reported outcome

Key secondary outcome(s))
1. Possible recurrent ICH
2. Symptomatic non-fatal extracerebral haemorrhage, extracranial haemorrhage, and vaso-occlusive events
3. Death
4. Modified Rankin Scale score
5. Adherence to antiplatelet drug(s)

1. Fatal events (i.e. followed by death within 30 days): complication of qualifying ICH; symptomatic extradural/subdural/subarachnoid/intraventricular haemorrhage; symptomatic major extracranial haemorrhage; symptomatic vaso-occlusive events; cardiac death with symptoms suggestive of myocardial ischaemia (type 3) or evidence of arrhythmia; deaths from any other known cause; rapidly fatal stroke, consistent with the clinical manifestations of ICH, but without radiographic or pathological confirmation; unwitnessed deaths without a clear cause and without further investigation.
2. Non-fatal events (i.e. not followed by death within 30 days): symptomatic extradural/subdural /subarachnoid/intraventricular haemorrhage; symptomatic major extracranial haemorrhage; symptomatic vaso-occlusive events; non-fatal stroke, with brain imaging performed too late to distinguish ICH from cerebral infarction.
Timepoint: over 2 years after baseline, detected using annual general practitioner and participant follow-up, with independent, blinded adjudication of the clinical information and investigations relating to every reported outcome

Annual ratings of participant function:
Simplified modified Rankin Scale postal questionnaire or Structured telephone interview with non-responders to the postal questionnaire, completed by the participant or their carer.

Completion date
28/02/2021

Eligibility

Key inclusion criteria
1. Patient age 18 years or over, either sex
2. Spontaneous intracerebral haemorrhage (ICH) not attributable to preceding traumatic brain

injury, on the basis of:
2.1. A history from the patient/witness of spontaneous symptom onset without preceding head trauma (head trauma occurring subsequent to ICH symptom onset is permissible)
2.2. brain imaging appearances consistent with spontaneous ICH (which may be accompanied by the brain/bone/soft tissue appearances of trauma occurring subsequently)
2.3. Either 'secondary' to an underlying structural cause (e.g. aneurysm, tumour, arteriovenous malformation, or intracranial venous thrombosis), or 'primary' (if the investigator either does not suspect an underlying structural cause, or it is not detected by further radiographic investigation)
3. Patient had taken an antithrombotic (i.e. anticoagulant or antiplatelet) drug for the prevention of vaso-occlusive disease for any length of time before the onset of the qualifying ICH.
4. Patient is at least 24 hours after ICH symptom onset (randomisation is expected to usually occur when they are approaching the end of their hospital admission/assessment for the qualifying ICH).
5. Patient and their doctor are both uncertain about whether to start or avoid antiplatelet drugs.
6. Patient is registered with a general practitioner (GP).
7. Brain imaging study that first diagnosed the qualifying ICH is available.
8. Consent to randomisation from the patient (or personal / legal / professional representative if the patient does not have mental capacity).
9. If eligible for the brain MRI sub-study, the MRI must be performed after the ICH but before randomisation.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
537

Key exclusion criteria
1. ICH due to traumatic brain injury, in the opinion of the investigator
2. ICH due to haemorrhagic transformation of an ischaemic stroke, in the opinion of the investigator
3. Patient is taking an anticoagulant drug following ICH
4. Patient is pregnant, breastfeeding, or of childbearing age and not taking contraception
5. Patient is being treated or followed up in another Clinical Trial of an Investigational Medicinal Product (CTIMP)
6. Patient and carer unable to understand spoken or written English (local translator is not available)

7. Patients are ineligible for the brain MRI sub-study if they are claustrophobic or they have a contraindication to MRI

Date of first enrolment
02/05/2013

Date of final enrolment
31/05/2018

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
122 Sites in the United Kingdom
United Kingdom
EH4 2XU

Sponsor information

Organisation
University of Edinburgh (UK) and NHS Lothian

ROR
https://ror.org/03q82t418

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (BHF) (UK)

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
A fully anonymised version of the dataset used for analysis of the main results and the final results with individual participant data and a data dictionary will be available on Datashare for other researchers to apply to use, via https://datashare.is.ed.ac.uk/handle/10283/3265. Written proposals will be assessed by members of the RESTART trial steering committee and a decision made about the appropriateness of the use of data. A data-sharing agreement will be put in place before any data are shared.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	29/06/2019	29/05/2019	Yes	No
Results article		08/06/2021	10/06/2021	Yes	No
Results article	Extended Follow-up	03/09/2021	06/09/2021	Yes	No
Protocol article	protocol	05/03/2018		Yes	No
Abstract results	Results abstract of extended follow-up European Stroke Organisation Conference 2021	03/09/2021	29/03/2023	No	No
HRA research summary			28/06/2023	No	No
Other publications	subgroup analyses	01/07/2019	17/02/2021	Yes	No
Other publications	Healthcare systems data accuracy compared with adjudicated questionnaire follow-up	16/11/2024	19/11/2024	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan	statistical analysis plan	25/03/2019	27/03/2019	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes